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Case Report

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Perioperative Implications of Vaping

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Abstract

Over the past 10 - 15 years, there has been a significant increase in the use of electronic cigarettes. These devices are generally used to deliver nicotine through inhalation by aerosolization. While the long-term risk of lung cancer is yet to be known, the chemicals and impurities in the solutions may have other acute and chronic effects on the respiratory system including respiratory failure from adult respiratory distress syndrome. Recent concerns have been raised regarding the potential for significant acute and chronic health care risks of these devices including pneumonitis, airway reactivity and respiratory failure. Given that many of the acute effects are related to the respiratory system, anesthetic care may be required during diagnostic procedures including bronchoscopy to investigate the etiology of acute respiratory symptomatology. We present an adolescent who presented to the operating room for bronchoscopy and bronchoalveolar lavage to investigate the etiology of respiratory involvement following an episode of vaping. The healthcare and end-organ effects of nicotine, tobacco smoke and vaping are discussed, and potential anesthetic implications are presented.

Keywords: Vaping; Tobacco; Airway reactivity; E-cigarettes

Introduction

In the last decade, pre-existing pulmonary diseases have been increasingly encountered in patients presenting for elective and emergency surgical procedures [1]. In the adolescent population, it is recognized that one cause of such issues is the introduction of electronic cigarettes. Electronic cigarettes were patented in China in 2003 and subsequently released in the United States in 2007 [2]. Although electronic cigarettes have many names, designs and a variety of different features, their basic components include a battery, electronic heater and liquid solution [3, 4]. In most cases, the electronic cigarette is used to deliver the addictive chemical, nicotine, through inhalation by aerosolization. Over the past decade, there has been a significant increase in the popularity and use of electronic cigarettes. The expansion of these products and their popularity has resulted in a multi-billion-dollar industry [3-5]. While electronic cigarettes were initially thought to be a mechanism for smoking cessation with elimination of some of the safety issues related to the inhalation of tobacco smoke, the long-term safety and health effects of these devices and the chemicals delivered require more research [6]. Electronic cigarettes and the chemicals in the solutions delivered may have widespread effects on the respiratory, immunologic and cardiovascular systems [2-4]. Another concern is the significant rate of use of these products by the adolescent population, which has been highly influenced by successful targeted marketing and the availability of a variety of flavored vaporization solutions. The use of electronic cigarettes with higher nicotine concentrations by youths may increase dependence and the subsequent frequency and intensity of smoking and vaping [7].

Recent concerns have been raised regarding the potential for significant acute and chronic health care risks of these devices including pneumonitis, airway reactivity and respiratory failure from adult respiratory distress syndrome (ARDS) [8]. These effects may be related to nicotine or to the diluent used for aerosolization. Given that many of the acute effects are related to the respiratory system, invasive procedures including bronchoscopy may be required when investigating the etiology of acute respiratory symptomatology. While these procedures frequently require anesthetic care, there is limited information on the perioperative implications of vaping. We present an adolescent who presented to the operating room for bronchoscopy and bronchoalveolar lavage (BAL) to investigate the etiology of respiratory involvement following an episode of vaping. The healthcare and end-organ effects of nicotine, tobacco smoke and vaping are discussed, and potential anesthetic implications are presented.

Case Report

A 16-year-old, 59-kg female adolescent presented for anesthetic care during bronchoscopy and BAL. Past medical history included familial porphyria cutanea tarda, protein S deficiency

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and environmental allergies for which she took levocetirizine, 5 mg daily. Past social history included living on a farm with multiple farm animals and hay, vaping, tetrahydrocannabinol (THC) inhalation and second-hand cigarette smoke exposure at home. Her past family history was positive for asthma, hematological disorders and polycystic ovary syndrome. She had originally presented to the emergency department (ED) with cough and difficulty breathing for 4 days and a 1-week history of chest pain. Prior to her ED admission, she was diagnosed with left lower lobe pneumonia and started on azithromycin by a physician at an urgent care clinic. She also had increased albuterol inhaler use (approximately 4 - 5 daily uses) without symptomatic relief. The respiratory symptoms worsened with exertion, heat exposure and lying supine. She also reported decreased oral intake and energy but denied fevers or rashes. Physical examination in the ED revealed tachypnea, diminished air entry bilaterally, inspiratory and expiratory wheezes, rales and labored breathing. Her vital signs were notable for a pulse of 111 beats/min, respiratory rate of 32 breaths/min, blood pressure of 122/82 mm Hg, temperature of 36.7 °C and oxygen saturation (SpO_2) of 91% on room air. A chest radiograph demonstrated multi-focal airspace disease suggestive of pneumonia with hilar lymphadenopathy. Pulmonary embolism was ruled out by computed tomography angiography (CTA) which showed normal main, branch, lobar and segmental pulmonary arteries with normal enhancement. However, the CTA did show bilateral hilar lymphadenopathy, the largest of which was 2.3 cm in dimension, and multi-focal airspace opacities in all lobes. The electrocardiogram revealed a prolonged QTc of 531 ms with T-wave abnormalities, so pediatric cardiology was consulted. A complete blood count was negative for leukocytosis but did show a left shift. Procalcitonin, hepatic function tests and urinalysis were unremarkable. Electrolytes, blood urea nitrogen and creatinine were normal except for mild hypokalemia (3 mEq/L). C-reactive protein and sedimentation rate were elevated on multiple tests. Treatment in the ED included inhaled albuterol-ipratropium, oral prednisone (60 mg) and ceftriaxone. Three months prior to this acute presentation, the patient had been diagnosed with pneumonia and multi-focal small airways disease, and at that time, the differential diagnosis included environmental exposure causing hypersensitivity pneumonitis as she had a history of tetrahydrocannabinol (THC) use by vaping, farm environment exposure and other infectious causes. During the previous visit, a complete blood count showed eosinophilia of 33% (reference range 1-4%) and a respiratory infection antigen array was negative. Sputum cultures showed mixed bacteria with purulent secretions. Fungal antibody panel showed rare *Candida albicans*. HIV 1 and 2 serology results were negative. Histoplasma, Blastomyces, Aspergillus antigens and antibodies were all negative. Legionella serology was negative, and a TB test was negative. Given the uncertain etiology of her recurrent lung disease, she was scheduled for bronchoscopy and BAL in the operating room. She was held *nil per os* for 6 h and transferred to the operating room where routine American Society of Anesthesiologists' monitors were placed. Anesthesia was induced with propofol and endotracheal intubation facilitated by the administration of rocuronium. Anesthesia was maintained with sevoflurane in air and oxygen. Bronchoscopic findings included profuse edema throughout the right and left tracheobronchial tree, mucopurulent mucus plugs in the left lower lobe and throughout the right tracheobronchial tree. She tolerated the procedure well with no intraoperative complications. After recovery in the post-anesthesia care unit, she was discharged to the inpatient ward without postoperative complications. BAL showed 61% eosinophils and Charcot-Leyden crystals without signs of parasitic larvae or eggs, consistent with the diagnosis of hypersensitivity pneumonitis or acute eosinophilic pneumonia. All subsequent cultures and the infectious disease work-up were negative. The patient's oxygen requirement postoperatively was stable at 2 L/min via nasal cannula. Following the procedure, the patient was started on systemic corticosteroids. Her oxygen requirement decreased, and she was weaned to room air over the next 48 - 72 h. She was later discharged home on postoperative day 4 on a prolonged corticosteroid course. After discharge, she remained compliant with the treatment plan. Her symptoms slowly resolved, and follow-up chest radiograph showed clearing of the pulmonary involvement. Spirometry conducted 2 months after the start of the corticosteroid regimen revealed a mild obstructive pattern that resolved with albuterol. A repeat complete blood count showed a normal white blood count of $7.1 \times 10^3/\mu L$ and decreased peripheral eosinophilia of 10.7% (reference range 1.0-4.0%). The patient reported a good state of health with no further symptoms after finishing the corticosteroid treatment regimen and continued cessation of vaping and THC use.

Discussion

Although the detrimental and addictive effects of tobacco (nicotine) use have been clearly demonstrated over the last few decades, tobacco remains the leading cause of preventable death globally [9]. There has been a gradual decline in global tobacco use due to preventive measures such as reduced access to cigarettes and increased public awareness on its risks including lung and other malignancies, chronic obstructive pulmonary disease (COPD), inflammatory bowel disease, acute kidney injury, osteoporosis and bone fractures, stroke and coronary artery disease [9-11]. Another reason for the decline in tobacco use has been a shift towards the use of other nicotine products such as electronic nicotine delivery systems (e-cigarettes) [12]. This shift has been encouraged and aided by aggressive promotion of e-cigarettes as smoking cessation aids; however, evidence-based medicine has not been able to provide adequate data to document their efficacy in this regard. Moreover, current research even suggests that the use of e-cigarettes may encourage the use of conventional cigarettes [13-15].

E-cigarettes use has increased for several reasons including reduced costs, perceived reduced toxicity, more freedom of use in smoke-free places, and to allow for smoking cessation. An especially important population within this shift from tobacco use to electronic nicotine systems (e-cigarettes) are adolescents. E-cigarette use among adolescents and high school students has increased significantly in the last decade to rates as high as 25% among high school students. Measurement of serum cotinine, a marker for tobacco use, has shown that there are significant similarities between the effects of e-cigarettes

and traditional cigarettes [16]. Although e-cigarettes reduce exposure to the harmful toxins in conventional tobacco and cigarette smoke, they introduce a new array of potential toxins in the diluents used to carry the nicotine [17]. They also expose the smoker to potentially higher levels of nicotine and thereby elevate its addiction potential [17].

The physiological effects from the use of e-cigarettes are numerous to both the users as well as non-users who are exposed to the vapor and the exhaled smoke. The aerosol from e-cigarettes may contain harmful substances and chemicals including ultrafine particles with flavoring such as diacetyl that cause serious lung disease, carcinogens, as well as heavy metals such as nickel, tin and lead. There are over 7,700 flavors available with more than 240 new flavors added every month [18]. Toxic chemicals may be used to increase the e-cigarette solution's colors, aromatic properties and scents in order to appeal to the adolescent population. Acute effects of e-cigarette use have been reported to involve the pulmonary, cardiovascular and immune systems.

Pulmonary effects of toxic chemicals within the solution include disturbances of the cough reflex, throat irritation, dry cough and increased chronic respiratory problems with an increased incidence of sinusitis and rhinitis. A recent study involving healthy smokers (n = 30, 14 men and 16 women with a mean age of 34.8 years) compared to a control group (n = 10) showed that a 5-min exposure to a e-cigarette cartridge led to immediate respiratory changes within the experimental group when comparing respiratory function tests before and after exposure including changes dynamic lung volume, exhaled nitric oxide levels and total respiratory resistance [19, 20]. The study cohort included patients ranging in age from 19 to 56 years with no history of lung disease, currently using no medications and no acute illnesses in the previous two weeks. Specific changes in the experimental group included a decreased fraction of exhaled nitric oxide, increased respiratory impedance, increased inspiratory flow resistance and increased overall peripheral airway resistance [19].

In addition to the respiratory effects related to diluent for e-cigarette use, the nicotine within the aerosol solution may cause vasoconstriction, decreased microvascular tissue perfusion and oxygenation, and increase the risk for cardiovascular disturbances. E-cigarette inhalation affects vascular function, specifically endothelial function and inhibits nitric oxide bioavailability leading to decreased vasodilation and increased platelet activation [15, 21, 22]. The nicotine within e-cigarette aerosol may activate the sympathetic nervous system, thereby resulting in vasoconstriction of the coronary blood vessels as well as increases in heart rate and blood pressure [22]. Animal studies have noted that nicotine increases the risk of arrhythmias by reducing the ventricular fibrillation threshold and promoting the development of ventricular fibrillation after experimental myocardial infarctions [22]. These changes and others have showcased nicotine's role in impaired heart remodeling, increased risk of heart failure, sudden cardiac death due to arrhythmias, and progressive heart failure due to cardiovascular disease [22, 23]. Overall, nicotine leads to increased hemodynamic instability through the increased release of catecholamines under general anesthesia. E-cigarettes may also increase the risk of nicotine toxicity due to the increased availability of high concentrations of nicotine in the e-cigarette solutions [24].

Nicotine toxicity during adolescence has recently been associated with significant neuronal deficits in auditory processing, working memory, attentiveness, with an increase in impulsivity [25]. Other studies and human case reports have shown decreased density and viability of Kupffer cells, increases in complement protein activation and deposition onto hepatic Kupffer cells, enhanced hydrogen peroxide production due to increased xanthine oxidase and peroxidase activity and ultimately increased reactive oxygen species [15, 26]. The potential deleterious physiologic implications of e-cigarette or vaping associated lung injury (EVALI) are significant with recent reports in the lay literature of death related to vaping and its associated lung injury.

During the perioperative period, e-cigarettes have recently been found to be associated with pro-inflammatory effects, increased cytotoxicity and decreased immune defenses, all leading to increased perioperative risk for patients undergoing surgical procedures [27]. Due to the physiological similarities of the effects of tobacco use and e-cigarette use, perioperative and postoperative considerations between the two appear to be similar [15]. For instance, heavy tobacco or e-cigarette uses are both associated with increased risk of systemic postoperative complications including wound dehiscence and surgical site infections [28, 29]. Additional postoperative complications of tobacco usage included venous thromboembolism, acute cardiac or cerebrovascular events, anemia, gastrointestinal bleeding, urinary tract infections and pneumonia [15, 28]. A recent analysis reported an increased postoperative complication rate (42.5% vs. 8.9%, $P < 0.001$) when comparing smokers to those who have never smoked, the majority of these being infection-related [29, 30]. Following spinal decompression and fusion, smoking has been shown to be an independent risk factor for infection [31]. Other common postoperative complications reported in smokers include pulmonary and cardiac related morbidity such as postoperative pneumonia, atelectasis, respiratory failure, myocardial infarction and arrhythmias. Smoking has also been shown to have transient effects on local tissue microenvironments leading to prolonged inflammation and defective reparative cell functioning which may result in delayed healing [32]. More superficially, a systematic review reported numerous perioperative changes result from smoking including an imbalance of proteolytic enzymes and their respective inhibitors, decreased tissue oxygenation and aerobic metabolism, reduced fibroblast proliferation and migration leading to the downregulation of collagen synthesis and deposition [32].

As with all anesthetic care, preoperative preparation begins with a thorough preoperative evaluation and identification of acute issues as well as chronic comorbid conditions. Although asking patients regarding their cigarette/tobacco usage is normal practice, inquiring specifically about e-cigarette usage has also become important as the various health effects of e-cigarette use need to be considered for patients undergoing anesthesia. Patients may deny tobacco use and yet continue e-cigarette use without considering its impact. As noted above, many of the effects and concerns of e-cigarette parallel those related to tobacco use [33]. Although abstinence from smoking is suggested prior to major surgical procedures, guidelines

regarding e-cigarette use have not been universally defined. Cessation of smoking for 4 - 6 weeks prior to a procedure has been shown to decrease the incidence of postoperative pulmonary complications [34-37]. However, cessation closer to the time of surgery may increase bronchorrhea and the incidence of perioperative respiratory complications.

When considering the end-organ effects of vaping and its potential perioperative implications, attention must be focused on both the chemical inhaled and the carrier solution. Nicotine affects hepatic microsomal enzymes and the activity of cytochrome P-450 mixed oxidase metabolic pathways, altering the pharmacokinetics and pharmacodynamics of many anesthetic agents [38]. E-cigarette use results in the production of toluene and other volatile organic compounds that possess central nervous system depressant effects which may alter a patient's anesthetic requirements [39]. In addition to the hepatic effects, nicotine in e-cigarettes increases airway resistance and impedance through direct stimulation of afferent pathways in the bronchial mucosa, triggering the parasympathetic cholinergic pathways leading to bronchoconstriction [19, 40].

Managing the patient with suspected EVALI may include hospitalization, to treat decreased O_2 saturation or respiratory insufficiency, the impact of which may be escalated in patients with comorbid respiratory conditions. Treatment plans may include corticosteroids to treat hypersensitivity pneumonitis and early initiation of antibiotics for community-acquired pneumonia. As noted in our patient, the most predominant acute effects related to the respiratory system and e-cigarette use were increased airway reactivity, presenting as bronchoconstriction, bronchospasm, and air-trapping, similar to obstructive airway with depressed pulmonary function [41]. Regardless of the etiology, increased airway reactivity should be acutely treated with albuterol. Given involvement of the cholinergic pathway, the addition of inhaled anticholinergic agents (ipratropium) may be useful [42]. Additionally, prior to endotracheal intubation, topical or intravenous lidocaine may be administered to suppress laryngeal hyper-reactivity. Warming and humidifying the inspired gases may also be helpful in reducing airway reactivity [43]. Acute treatment of intraoperative bronchospasm may respond to deepening the level of anesthesia or inhaled β-adrenergic agonists [44]. Refractory cases may require intravenous epinephrine, ketamine or magnesium [42]. In particular, the volatile anesthetics such as sevoflurane and isoflurane produce significantly sustained bronchodilation [45]. Patients should be counseled on the negative effects of e-cigarette use on recovery including the potential for increased postoperative respiratory issues, decreased wound healing and an increased incidence of postoperative infections. When considering the effects of e-cigarette use on the perioperative course, attention should be directed toward both the diluent and the chemical inhaled. These agents may have significant end-organ effects due to their direct irritant properties as well as the profound physiologic effects of the chemicals inhaled.

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Conflict of Interest

None to declare.

Informed Consent

In accordance with IRB of Nationwide Children's Hospital, need for documentation of informed consent waved.

Author Contributions

Amogha Krishna contributed to incorporation of edits, preparation of secondary and final drafts. Wana Mathieu contributed to preparation of initial drafts, review of final manuscript. Eric Mull provided direct patient care, review of final manuscript. Joseph Tobias contributed to concept, review of all drafts.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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